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Pilot Production of Mesenchymal Stem/Stromal Freeze-Dried Secretome for Cell-Free Regenerative Nanomedicine: A Validated GMP-Compliant Process.

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Abstract

In this paper, a pilot production process for mesenchymal stem/stromal freeze-dried secretome was performed in a validated good manufacturing practice (GMP)-compliant cell factory. Secretome was purified from culture supernatants by ultrafiltration, added to cryoprotectant, lyophilized and characterized. We obtained a freeze-dried, "ready-off-the-shelf" and free soluble powder containing extracellular vesicles and proteins. In the freeze-dried product, a not-aggregated population of extracellular vesicles was detected by nanoparticle tracking analysis; Fourier transform infrared spectra showed the simultaneous presence of protein and lipids, while differential scanning calorimetry demonstrated that lyophilization process successfully occurred. A proteomic characterization allowed the identification of proteins involved in immune response, response to stress, cytoskeleton and metabolism. Moreover, the product was not cytotoxic up to concentrations of 25 mg/mL (on human fibroblasts, chondrocytes and nucleus pulposus cells by MTT assay) and was blood compatible up to 150 mg/mL. Finally, at concentrations between 5 and 50 mg/mL, freeze-dried secretome showed to in vitro counteract the oxidative stress damage induced by H_2O_2 on nucleus pulposus cells by MTT assay.

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Extracellular vesicle and mesenchymal stem cells in bone regeneration: recent progress and perspectives.

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Abstract

Transplanting mesenchymal stem cells (MSCs) has been widely perceived as an ideal treatment for bone repair and regeneration, owing to their differential potential. However, researchers found that very few intravenous MSCs could stay in the target tissue, whereas the majority of them are trapped in liver, spleen, and lung, largely reducing its therapeutic effects. Recently, extracellular vesicles (EVs) have attracted increased attention due to their function in bone repair and advantages over traditional cell therapy. Also, MSCs-derived EVs are likely to achieve the osteogenic goal via modulating the cells and cytokines involved in bone metabolism. This review aims at summarizing the function of EVs and MSCs in bone metabolism and regeneration.

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Gene expression profiling of human bone marrow mesenchymal stem cells during osteogenic differentiation.

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Abstract

OBJECTIVE:

Osteogenesis is a multiple-step process through which osteoblasts are derived from bone marrow mesenchymal stem cells (MSCs) with multilineage differentiation potential. This study aimed to analyze gene expression profiling during osteogenic differentiation of MSCs.

MATERIALS AND METHODS:

Human MSCs were isolated and induced for differentiation in osteogenic medium. Full-genome gene expression microarrays and gene ontology analysis were performed.

RESULTS:

A total of 1,680 differentially expressed genes in differentiated MSCs were identified including 430 upregulated and 1,250 downregulated. Moreover, pathway-act-network analysis showed that cell cycle, p53 signaling pathway and focal adhesion, had high degree (>5). The ribonucleotide reductase M1, thymidine kinase 1 and histone cluster 1 H3e also showed high degree (>10). Polymerase chain reaction analysis confirmed the differential expression of insulin-like growth factor binding protein 3, SMAD family member 3, transforming growth factor beta 2, and fibroblast growth factor 14 in differentiated MSCs.